

AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [0102] at page 7 of the published patent application (US Patent Application Publication No. US 2006/0185025 A1) with the following rewritten paragraph:

For human chromosome 21, nucleotide sequences for the entire long arm and part of the short arm excluding the centromere region have been disclosed in public database (for example, refer to <http://hgp.gsc.riken.go.jp/chr21/index.html> (Riken Genomic Sciences Center, Human Genome Research Group)). By utilizing such sequence information, it will be possible to insert artificial telomere sequence or loxp sequence described later in a site-specific manner by homologous recombination. In addition, chromosome 21 of about 48 Mb will be decreased one third to about 16 Mb after deleting the distal region of the long arm, and a HAC vector of about 2 Mb which contains no known genes will be finally constructed after deleting the distal regions of the long and short arms.

Please replace paragraph [0117] at page 8 of the published patent application (US Patent Application Publication No. US 2006/0185025 A1) with the following rewritten paragraph:

In addition, when, for example, the sequence of the long arm of human chromosome 14 is deleted at a site nearer to the centromere than the site in SC20, the target sequence can be designed based on the nucleotide sequence within the AL157858 region such that telomere truncation will occur on the telomere side of the target sequence, thus cutting off the distal region of the long arm at the site used to design the target sequence. In addition, when, for example, deleting the distal region of the short arm, the target sequence may be designed based on a nucleotide sequence within the 14p region of human chromosome 14, preferably a nucleotide sequence within the 14p12 region, more preferably the nucleotide sequence of OR4H12, OR4Q4, RNR2, OR4LI, RNU6C, FDP3L3, K12T, C14orf57, OR6S1, M195, OR4K14, MGC27165, LCH, OR10G3, OR4K3, OR4E2, H1RNA, ATP5C2, OR11H6 or OR4M1 (~~online genome database~~ (<http://www.ncbi.nlm.nih.gov/mapview/maps.cgi?ORG=hum&CHR=14&BEG=0.00&END=>) provided by the US National Center for Biotechnology Information (NCBI)). Those skilled in the art can design the target sequence as appropriate so as to produce a desired HAC vector without limitation to the region described above.

Please replace paragraph [0118] at page 8 of the published patent application (US Patent Application Publication No. US 2006/0185025 A1) with the following rewritten paragraph:

In addition, when, for example, the sequence of the long arm of an intact human chromosome 14 is to be deleted, the target sequence can be designed based on a nucleotide sequence within the 14q region, preferably the nucleotide sequence at AL512310 (GenBank Accession number) such that telomere truncation will occur on the telomere side of the target sequence, thus cutting off the distal region of the long arm at the site used to design the target sequence. In addition, when, for example, deleting the distal region of the short arm, the target sequence may be designed based on a nucleotide sequence within the 14p region of human chromosome 14, preferably a nucleotide sequence within the 14p12 region, more preferably the nucleotide sequence of OR4H12, OR4Q4, RNR2, OR4L1, RNU6C, FDPSL3, K12T, C14orf57, OR6S1, M195, OR4K14, MGC27165, LCH, OR10G3, OR4K3, OR4E2, H1RNA, ATP5C2, OR11H6 or OR4M1 (online genome database (~~http://www.ncbi.nlm.nih.gov/mapview/maps.cgi?ORG=hum&CHR=14&BEG=0.00&END~~) provided by the US National Center for Biotechnology Information (NCBI)). Those skilled in the art can design the target sequence as appropriate so as to produce a desired HAC vector without limitation to the region described above.

Please replace paragraph [0150] at page 11 of the published patent application (US Patent Application Publication No. US 2006/0185025 A1) with the following rewritten paragraph:

In addition, the cells used as raw material for gene and cell therapy and tissue regeneration therapy for humans should be normal cells but not immortalized cells in light of safety to avoid canceration. While there are a number of cases of transfer of chromosomes to immortalized cells and cancerous cells in humans and other animals, there is no reported case of transfer of chromosomes to normal somatic cells as far as the on-line literature database PubMed (~~http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed~~) of the US National Center for Biotechnology Information (NCBI) was searched for the keywords: chromosome, transfer, human, normal, primary or somatic and cell, excepting the report of transfer to bovine fetal normal fibroblast (Kuroiwa et al., Nature Biotech., 20: 889, 2002). Consequently, a general recognition has been that transferring chromosomes to human normal somatic cells is difficult.

Please replace paragraph [0238] at page 17 of the published patent application (US Patent Application Publication No. US 2006/0185025 A1) with the following rewritten paragraph:

(E-4) Although it is not intended to limit indications, the method of the invention can be used to produce the HAC vector into which the causal gene for a single-gene disorder, for example .alpha.-1 antitrypsin deficiency, cystic fibrosis (CFTR), chronic granulomatous disease, familial hypercholesterolemia, Fanconi's anemia, Gaucher's disease, Hunter's syndrome, ornithine transcarbamylase deficiency, purine nucleotide phosphorylase deficiency, ADA-SCID, leukocyte adhesion deficiency, Canavan disease, callosum atrophy, Fabry's disease and amyotrophic lateral sclerosis, and, although it is not intended to limit the method of administration to patients, the HAC vector can be transferred to, for example, human cells and transplanted to patients to recruit the deficient molecules. For information on disease causing genes, see the on-line literature database PubMed (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>) of the US National Center for Biotechnology Information (NCBI) or OMIMTM - ~~Online~~ **Online** Mendelian Inheritance in ManTM (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>).

Please replace paragraph [0257] at page 19 of the published patent application (US Patent Application Publication No. US 2006/0185025 A1) with the following rewritten paragraph:

The sequences of primer oligonucleotides for these STS markers can be available by accessing to the on-line database: UniSTS (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=unists>) of the National Center for Biotechnology Information of the United States. The Registration Numbers of the aforementioned 6 types of STS markers are UniSTS: 76223, 45641, 54124, 22625, 54266, and 53746 sequentially in the order. Besides these, the sequences of primer oligonucleotides for the genes, which were designed based on the nucleotide sequence obtained from the GenBank database, are shown below: